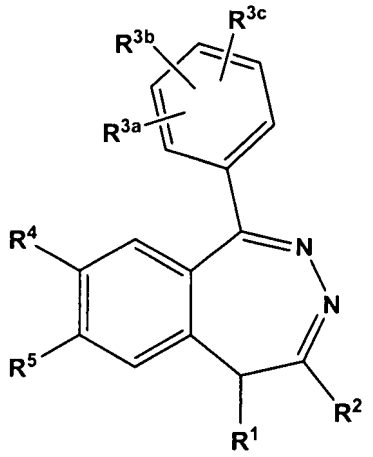
Amendments to the Claims

The following listing of claims replaces all prior versions, and listings, of claims in the application.

Listing of Claims

1. (currently amended) A method of lowering body temperature of an individual in need thereof, comprising administering to the individual an effective amount of at least one compound according to Formula I:



I

wherein:

R^1 is -(C_1-C_7)hydrocarbyl or -(C_2-C_6)heteroalkyl;

R^2 is selected from the group consisting of –H, and -(C_1-C_7)hydro-carbyl;

wherein R^1 and R^2 may combine to form a carbocyclic or heterocyclic 5- or 6-membered ring;

R^{3a}, R^{3b} and R^{3c} are independently selected from the group consisting of –H, –O(C_1-C_7)hydrocarbyl, -OH, -OC(=O)(C_1-C_6)alkyl, -OC(=O)O(C_1-C_7)hydrocarbyl, -SH, –S(C_1-C_3)alkyl, –NH_2, -NH(C_1-C_6)alkyl, -N((C_1-C_6)alkyl)$_2$, -NH(=O)(C_1-C_6)alkyl, -NO_2, and halogen;

provided at least one of R^{3a}, R^{3b} and R^{3c} is other than –H;

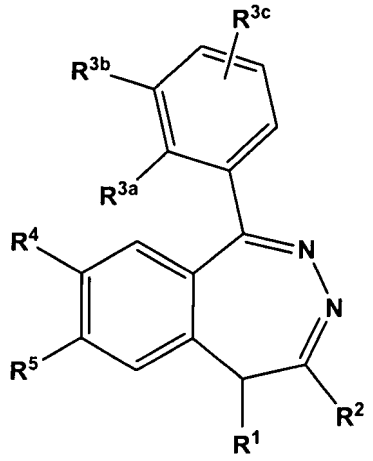
R^4 and R^5 are independently selected from the group consisting of –O(C_1-C_7)hydrocarbyl, -OH, -OC(=O)(C_1-C_6)alkyl, -OC(=O)O(C_1-C_7)hydrocarbyl, -SH, –S(C_1-C_3)alkyl, –NH_2, -NH(C_1-C_6)alkyl, -N((C_1-C_6)alkyl)$_2$, -NH(=O)(C_1-C_6)alkyl, -NO_2, and halogen;

wherein R^4 and R^5 may combine to form a 5-, 6- or 7-membered heterocyclic ring; and

wherein the administered compounds according to Formula I comprise an (*S*)-enantiomer, substantially free of the corresponding (*R*)-enantiomer, with respect to the absolute conformation at the 5-position of the benzodiazepine ring; or

a pharmaceutically-acceptable salt of such a compound.

2. (original) The method according to claim 1 wherein the administered compound is a compound according to Formula II:



II

wherein:

R^1 is -(C_1-C_7)hydrocarbyl or -(C_2-C_6)heteroalkyl;

R^2 is selected from the group consisting of –H, and -(C_1-C_7)hydro-carbyl;

wherein R^1 and R^2 may combine to form a carbocyclic or heterocyclic 5- or 6-membered ring;

R^{3a}, R^{3b} and R^{3c} are independently selected from the group consisting of –H, –O(C_1-C_7)hydrocarbyl, -OH, -OC(=O)(C_1-C_6)alkyl, -OC(=O)O(C_1-C_7)hydrocarbyl, -SH, –S(C_1-C_3)alkyl, $–NH_2$, -NH(C_1-C_6)alkyl, -N((C_1-C_6)alkyl)$_2$, -NH(=O)(C_1-C_6)alkyl, -NO_2, and halogen;

provided at least one of R^{3a} and R^{3b} is other than –H;

R^4 and R^5 are independently selected from the group consisting of –O(C_1-C_7)hydrocarbyl, -OH, -OC(=O)(C_1-C_6)alkyl, -OC(=O)O(C_1-C_7)hydrocarbyl, -SH, –S(C_1-C_3)alkyl, $–NH_2$, -NH(C_1-C_6)alkyl, -N((C_1-C_6)alkyl)$_2$, -NH(=O)(C_1-C_6)alkyl, -NO_2, and halogen;

wherein R^4 and R^5 may combine to form a 5-, 6- or 7-membered heterocyclic ring; and

wherein the administered compounds according to Formula I comprise an (*S*)-enantiomer, substantially free of the corresponding (*R*)-enantiomer, with respect to the absolute conformation at the 5-position of the benzodiazepine ring; or

a pharmaceutically-acceptable salt of such a compound.

3. (original) The method according to claim 2;

wherein:

R^{3c} is –H;

one or two of R^{3a}, R^{3b}, R^4, and R^5 is –OH; and

the remaining members of the group R^{3a}, R^{3b}, R^4, R^5 are independently selected from the group consisting of –O(C_1-C_7)hydrocarbyl, -OC(=O)(C_1-C_6)alkyl, -OH, -SH, –S(C_1-C_3)alkyl, –NH_2, -NH(C_1-C_6)alkyl, -N((C_1-C_6)alkyl)$_2$, -NH(=O)(C_1-C_6)alkyl, -NO_2, and halogen;

wherein R^4 and R^5 may combine to form a 5-, 6- or 7-membered heterocyclic ring.

4. (original) The method according to claim 3,

wherein:

one or two of R^{3a}, R^{3b}, R^4, and R^5 is –OH;

one of the remaining members of the group R^{3a}, R^{3b}, R^4, and R^5 is –O(C_1-C_7)hydrocarbyl; and

the remaining members of the group R^{3a}, R^{3b}, R^4, and R^5 are independently selected from the group consisting of –O(C_1-C_7)hydrocarbyl, -OC(=O)(C_1-C_6)alkyl, -SH, –S(C_1-C_3)alkyl, –NH_2, -NH(C_1-C_6)alkyl, -N((C_1-C_6)alkyl)$_2$, -NH(=O)(C_1-C_6)alkyl, -NO_2 and halogen;

wherein R^4 and R^5 may combine to form a 5-, 6- or 7-membered heterocyclic ring.

5. (original) The method according to claim 4,

wherein:

one or two of R^{3a}, R^{3b}, R^4, and R^5 is –OH; and

the remaining members of the group R^{3a}, R^{3b}, R^4, and R^5 are independently selected from the group consisting of –O(C_1-C_7)hydrocarbyl.

6. (original) The method according to claim 5,

wherein:

the compound according to Formula II is selected from the group consisting of:

(*S*)-1-(3,4-dimethoxyphenyl)-4-methyl-5-ethyl-7-hydroxy-8-methoxy-5H-2,3-benzodiazepine;

(*S*)-1-(3-hydroxy-4-methoxyphenyl)-4-methyl-5-ethyl-7,8-dimethoxy-5H-2,3-benzodiazepine;

(*S*)-1-(3-methoxy-4-hydroxyphenyl)-4-methyl-5-ethyl-7,8-dimethoxy-5H-2,3-benzodiazepine;

(*S*)-1-(3,4-dimethoxyphenyl)-4-methyl-5-ethyl-7-methoxy-8-hydroxy-5H-2,3-benzodiazepine;

(*S*)-1-(3-methoxy-4-hydroxyphenyl)-4-methyl-5-ethyl-7-hydroxy-8-methoxy-5H-2,3-benzodiazepine;

(*S*)-1-(3-hydroxy-4-methoxyphenyl)-4-methyl-5-ethyl-7-hydroxy-8-methoxy-5H-2,3-benzodiazepine; and

pharmaceutically-acceptable salts of such compounds.

7. (original) The method according to claim 2

wherein:

R^{3c} is –H; and

R^{3a}, R^{3b}, R^4, and R^5 are independently selected from the group consisting of –O(C_1-C_7)hydrocarbyl.

8. (original) A method according to claim 7, wherein the administered compound is (*S*)-tofisopam, or a pharmaceutically-acceptable salt thereof.

9. (original) The method according to claim 1 wherein said individual is afflicted with a disorder associated with an elevated body temperature.

10. (original) The method according to claim 9 wherein the disorder is fever.

11. (original) The method according to claim 9 wherein the disorder is malignant hyperthermia.

12. (original) The method according to claim 9 wherein the disorder is serotonin syndrome.

13. (original) The method according to claim 9 wherein the disorder comprises hot flashes.

14. (original) The method according to claim 13 wherein said hot flashes occur during menopause.

15. (original) The method according to claim 13 wherein said hot flashes occur during perimenopause.

16. (original) The method of claim 13 wherein said hot flashes are side effects of drug therapy.

17. (original) The method of claim 13 wherein said hot flashes occur subsequent to the removal of estrogen-producing tissue.

18. (original) The method of claim 13 wherein said hot flashes occur subsequent to organ failure of estrogen-producing organs.

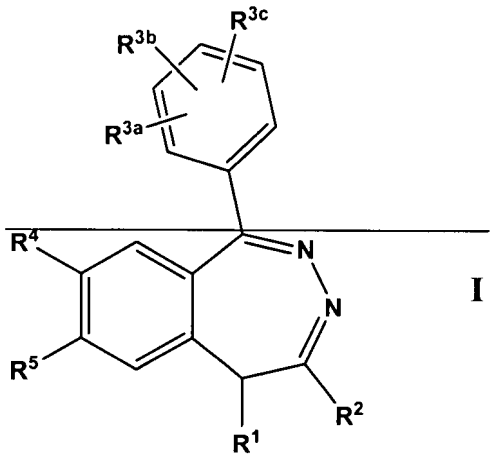
19. (original) The method of claim 1 wherein said individual is afflicted with a disorder wherein therapeutic benefit is achieved by lowering of the body temperature to a level below the normal body temperature.

20. (original) The method of claim 19 wherein the disorder is cerebral ischemia.

21. (original) The method of claim 19 wherein the disorder is stroke.

22. (currently amended) A method of lowering body temperature according to claim 1 wherein the individual in need thereof is ~~of~~ an individual suffering from hot flashes associated with menopause~~,~~ wherein the method further comprises ~~comprising~~ administering to said individual an effective amount of

~~(a) at least one compound according to Formula I:~~



I

~~wherein:~~

~~R^1 is $(C_1$-$C_7)$hydrocarbyl or $(C_2$-$C_6)$heteroalkyl;~~

~~R^2 is selected from the group consisting of H, and $(C_1$-$C_7)$hydro-carbyl;~~

~~wherein R^1 and R^2 may combine to form a carbocyclic or heterocyclic 5- or 6-membered ring;~~

~~R^{3a}, R^{3b} and R^{3c} are independently selected from the group consisting of H, $O(C_1$-$C_7)$hydrocarbyl, OH, $OC(=O)(C_1$-$C_6)$alkyl, $OC(=O)O(C_1$-$C_7)$hydrocarbyl, SH, $S(C_1$-$C_3)$alkyl, NH_2, $NH(C_1$-$C_6)$alkyl, $N((C_1$-$C_6)alkyl)_2$, $NH(=O)(C_1$-$C_6)$alkyl, NO_2, and halogen;~~

~~provided at least one of R^{3a}, R^{3b} and R^{3c} is other than H;~~

~~R^4 and R^5 are independently selected from the group consisting of $O(C_1$-$C_7)$hydrocarbyl, OH, $OC(=O)(C_1$-$C_6)$alkyl, $OC(=O)O(C_1$-$C_7)$hydrocarbyl, SH, $S(C_1$-$C_3)$alkyl, NH_2, $NH(C_1$-$C_6)$alkyl, $N((C_1$-$C_6)alkyl)_2$, $NH(=O)(C_1$-$C_6)$alkyl, NO_2, and halogen;~~

~~wherein R^4 and R^5 may combine to form a 5-, 6- or 7-membered heterocyclic ring; and~~

~~wherein the administered compounds according to Formula I comprise an (*S*) enantiomer, substantially free of the corresponding (*R*) enantiomer, with respect to the absolute conformation at the 5-position of the benzodiazepine ring; or~~

~~a pharmaceutically acceptable salt of such a compound; and~~

~~(b)~~ one or more additional therapeutic agents selected from the group consisting of estrogen agonists, progesterone agonists, selective estrogen receptor modulators, bisphosphonates, selective serotonin reuptake inhibitors, norepinephrine serotonin reuptake inhibitors and gamma aminobutyric ~~aminobuteric~~ acid modulators.

23. (original) The method according to claim 22, wherein the one or more additional therapeutic agents comprises an estrogen agonist and a progesterone agonist.

24. (currently amended) The method according to claim 22 or claim 23, wherein the one or more therapeutic agents comprises an estrogen agonist wherein the estrogen agonist is estradiol.

25. (currently amended) The method according to claim 22 or 23, wherein the one or more therapeutic agents comprises a progesterone agonist wherein the progesterone agonist is trimegestrone.

26. (currently amended) The method according to claim 22, wherein the one or more therapeutic agents comprises a selective estrogen receptor modulator ~~agonist is~~ selected from the group consisting of raloxifene and bazedoxifene.

27. (currently amended) The method according to claim 22, wherein the one or more therapeutic agents comprises a bisphosphonate [[is]] selected from the group consisting of risedronic acid and ibandronic acid.

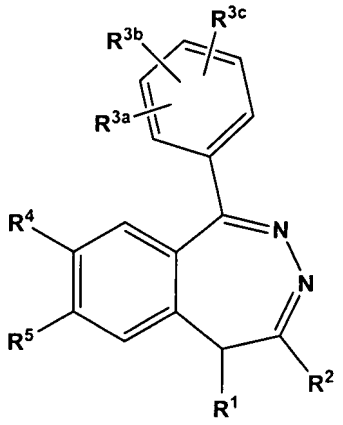
28. (currently amended) The method according to claim 22, wherein the one or more therapeutic agents comprises a selective serotonin reuptake inhibitor [[is]] selected from the group consisting of fluoxetine and paroxetine.

29. (currently amended) The method according to claim 22, wherein the one or more therapeutic agents comprises a norepinephrine serotonin reuptake inhibitor wherein the norephiephrine serotonin reuptake inhibitor is venlafaxine.

30. (currently amended) The method according to claim 22, wherein the one or more therapeutic agents comprises a gamma aminobutyric acid ~~GABA~~ modulator wherein the gamma aminobutyric acid modulator is gabapentin.

31. (currently amended) A composition comprising

(a) at least one compound of Formula I:



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wherein:

R^1 is -(C_1-C_7)hydrocarbyl or -(C_2-C_6)heteroalkyl;

R^2 is selected from the group consisting of –H, and -(C_1-C_7)hydro-carbyl;

wherein R^1 and R^2 may combine to form a carbocyclic or heterocyclic 5- or 6-membered ring;

R^{3a}, R^{3b} and R^{3c} are independently selected from the group consisting of –H, –O(C_1-C_7)hydrocarbyl, -OH, -OC(=O)(C_1-C_6)alkyl, -OC(=O)O(C_1-C_7)hydrocarbyl, -SH, –S(C_1-C_3)alkyl, $–NH_2$, -NH(C_1-C_6)alkyl, -N((C_1-C_6)alkyl)$_2$, -NH(=O)(C_1-C_6)alkyl, -NO_2, and halogen;

provided at least one of R^{3a}, R^{3b} and R^{3c} is other than –H;

R^4 and R^5 are independently selected from the group consisting of –O(C_1-C_7)hydrocarbyl, -OH, -OC(=O)(C_1-C_6)alkyl, -OC(=O)O(C_1-C_7)hydrocarbyl, -SH, –

$S(C_1\text{-}C_3)$alkyl, $-NH_2$, $-NH(C_1\text{-}C_6)$alkyl, $-N((C_1\text{-}C_6)\text{alkyl})_2$, $-NH(=O)(C_1\text{-}C_6)$alkyl, $-NO_2$, and halogen;

wherein R^4 and R^5 may combine to form a 5-, 6- or 7-membered heterocyclic ring; and

wherein the administered compounds according to Formula I comprise an (*S*)-enantiomer, substantially free of the corresponding (*R*)-enantiomer, with respect to the absolute conformation at the 5-position of the benzodiazepine ring; or

a pharmaceutically-acceptable salt of such a compound; and

(b) at least one additional therapeutic agent selected from the group consisting of estrogen agonists, progesterone agonists, selective estrogen receptor modulators, bisphosphonates; selective serotonin reuptake inhibitors, norepinephrine serotonin reuptake inhibitors and gamma aminobutyric ~~aminobuteric~~ acid modulators.